

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

### **Listing of the claims:**

- 1-28 (Canceled)
29. (New) An isolated polynucleotide that encodes a polypeptide comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated I $\kappa$ B.
30. (New) An antisense polynucleotide comprising at least 10 consecutive nucleotides complementary to a polynucleotide according to claim 29.
31. (New) An expression vector comprising a polynucleotide according to claim 29.
32. (New) A host cell transformed or transfected with an expression vector according to claim 31.
33. (New) A pharmaceutical composition comprising:
  - a) an isolated human E3 ubiquitin ligase polypeptide, said E3 ubiquitin ligase polypeptide comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated I $\kappa$ B, such that the polypeptide enhances ubiquitination of phosphorylated I $\kappa$ B; and
  - b) a physiologically acceptable carrier.
34. (New) An isolated antibody, or antigen binding fragment thereof that binds to a human E3 ubiquitin ligase sequence recited in SEQ ID NO:16.
35. (New) An antibody or fragment thereof according to claim 34, wherein the antibody is a monoclonal antibody.
36. (New) A pharmaceutical composition comprising an antibody or fragment thereof according to claim 34, in combination with a physiologically acceptable carrier.
37. (New) A method for modulating NF- $\kappa$ B activity in a patient comprising administering to a patient a pharmaceutical composition according to claim 33, wherein said pharmaceutical composition is in an amount sufficient to modulate NF- $\kappa$ B activity in the patient.

38. (New) A method according to claim 16, wherein the disorder is selected from the group consisting of inflammatory diseases, autoimmune diseases, cancer and viral infection.

39. (New) A method for screening for an agent that modulates NF- $\kappa$ B activity comprising the steps of:

a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide comprising a variant of SEQ ID NO:16 that differs therefrom at no more than 10% of the amino acid residues of SEQ ID NO:16 wherein said variant retains the ability to ubiquitination of phosphorylated I $\kappa$ B, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent; and

b) determining whether the polypeptide enhances ubiquitination of phosphorylated I $\kappa$ B, relative to a predetermined ability of the polypeptide to enhance ubiquitination of phosphorylated I $\kappa$ B in the absence of the candidate agent, and, if so;

c) identifying an agent that modulates NF- $\kappa$ B activity.

40. (New) A method according to claim 39, wherein the candidate agent is a small molecule.

41. (New) A method for screening for an agent that modulates NF- $\kappa$ B activity comprising the steps of:

a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide comprising a variant of SEQ ID NO:16 that differs therefrom at no more than 10% of the amino acid residues of SEQ ID NO:16 wherein said variant retains the ability to enhance ubiquitination of phosphorylated I $\kappa$ B, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent;

b) determining whether the polypeptide enhances ubiquitination of phosphorylated I $\kappa$ B, relative to a predetermined ability of the polypeptide to enhance ubiquitination of phosphorylated I $\kappa$ B in the absence of the candidate agent, and, if so;

c) identifying an agent that modulates NF- $\kappa$ B activity.

42. (New) A method for screening for an agent that modulates NF- $\kappa$ B activity comprising the steps of:

a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated I $\kappa$ B, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent;

- b) determining whether the polypeptide binds phosphorylated I $\kappa$ B or a phosphorylated I $\kappa$ B peptide comprising SEQ ID NO:8 or SEQ ID NO:9, and if so;
- c) identifying an agent that modulates NF- $\kappa$ B activity.

43. (New) A method for screening for an agent that modulates NF- $\kappa$ B activity comprising the steps of:

- a) contacting a candidate agent with an isolated human E3 ubiquitin ligase polypeptide comprising SEQ ID NO:16 or a truncated portion thereof of at least 50 amino acid residues wherein said portion retains the ability to enhance ubiquitination of phosphorylated I $\kappa$ B, under conditions and for a time sufficient to permit interaction between the polypeptide and candidate agent;

- b) determining whether the polypeptide modulates the release of NF- $\kappa$ B from I $\kappa$ B or the nuclear translocation of NF- $\kappa$ B, and if so;

- c) identifying an agent that modulates NF- $\kappa$ B activity.